BENJAMIN ELDER: So, first, I'd like to thank the Chiari and Syringomyelia Foundation for inviting us to give the lecture and for visiting here. So I'd like to talk about adult-onset hydrocephalus in this lecture.

So objectives of this talk are really to review the diagnosis, treatment options, outcomes. As well as complications of idiopathic normal pressure hydrocephalus, as well as idiopathic intracranial hypertension, which are two of the more common adult-onset variations of hydrocephalus. And then, finally, to review some of the CSF diversion strategies and shunt design that's been used over the years.

So starting with idiopathic normal pressure hydrocephalus, or iNPH. This etiology was first described by Hakim and Adams back in 1965. That includes the clinical triad of dementia, gait disturbance, and urinary incontinence that occurs with ventricular dilation and normal CSF pressures, with symptoms that are reversed by CSF diversion or shunt surgery.

There's forms of secondary normal pressure hydrocephalus, which can occur from subarachnoid hemorrhage or meningitis. As compared to idiopathic NPH, where it's really unknown. So that's the primary form that we deal with, and I'll be talking about this evening.

So there are new, updated guidelines in 2011 that came out of Japan. For these, they reviewed almost 1,500 publications on the diagnosis, and almost 1,000 publications on the treatment, to come up with some standardized recommendations in managing these patients.

So looking at NPH, again, there's a classification where it's divided into idiopathic NPH, which is the primary form that occurs from some unknown reason. As well as secondary NPH, which are from either acquired etiologies, or congenital or developmental etiologies. Within idiopathic NPH, it can be varied between what's called DESH-- or diffusely enlarged subarachnoid space hydrocephalus-- and non-DESH phenotypes. We'll talk about, in a moment, really what characterizes DESH versus the non-DESH phenotypes.

So in looking at the prevalence, most studies in the prevalence of idiopathic NPH have really looked at more of the hospital populations or a group of hospitals. The problem with a lot of these is that diagnosis really requires exam of the CSF with a spinal tap, which is an invasive procedure. There's very rare population-based studies that have been performed. And it, also, remains undetermined if there's difference in prevalence and incidence of idiopathic NPH between different ethnicities and races.

When we look at some of the limited population-based data, in Japan, there's some reasonably performed studies that are performed on the elderly community populations in different cities. If you look at the diagnosis based on imaging criteria, and having at least one of the symptoms of NPH, the prevalence was up to 3% in residents above 65 years, and 0.5% in those above 61 years.

Some of the limitation of this study is that the data may overestimate the prevalence. They didn't perform any CSF exam or a lumbar puncture. So these really only represent possible cases of iNPH. But if we translate that 3% number to the United States, where there's many millions of patients above age 65, those numbers are pretty staggering for people who may be suffering from this.

There's, also, what's called a AVIM, or A-V-I-M, which is asymptomatic ventriculomegaly with features of iNPH on an MRI. Where patients don't have any of the symptoms, but do have the signs on an MRI of enlarged ventricles. So there's some thought that this might represent a pre-clinical stage of iNPH, rather than just plain atrophy as we see in the elderly population. And over a follow-up period of a number of years, about 25% of these went on to develop dementia or gait problems.

Now, there are studies showing smaller numbers. So in a Norwegian study, they looked at the prevalence of NPH among the population covered by the hospital, and found that it was about 0.2%. Which was significantly different than in the Japanese study.

In another study, there is prevalence of up to 3 and 1/2% among a series of 400 patients, who were referred to a memory clinic for work up. And up to almost 20% among residents suspected of potentially having Parkinson's disease. So the numbers are probably somewhere in that low percent range. But, again, there's wide variation depending on the at-risk population.

So there are some risk factors for iNPH that have been identified, including hypertension, diabetes, low serum HDL. As well as age greater than 60, which is really the cutoff for the diagnosis of iNPH. But a lot of these are associated with vascular problems, so it suggests that there may be some vascular changes involved in the pathogenesis.

So, again, why does NPH or iNPH develop? We don't really know. This was a slide I borrowed from Dr. Mark Luciano at Johns Hopkins. But it really shows that there's many mechanisms of

CSF drainage. And it's a much more complicated pathway than we initially thought. There's newer cerebral emphatic systems, the glymphatic system, as well as capillary exchange that can all occur. And so there's likely changes that go on throughout this pathway that can lead to idiopathic normal pressure hydrocephalus.

Unfortunately, we don't have any clear pathogenesis worked out yet. But there are some patterns that have been developed, with thickening and fibrosis of the leptomeninges, inflammation around the arachnoid granulations, some disruption of the ventricular ependymal, as well as subependymal gliosis. And there are some pathological changes that are also seen in Alzheimer's disease, with senile plaques and neurofibrillary tangles. But, really, it's a clinical diagnosis of iNPH right now.

So the classic triad is, again, gait disturbance, urinary incontinence, and cognitive dysfunction. Most people believe that gait dysfunction has to occur in prior studies. They say it's 91% to 100%. But some people feel that should be in 100% of cases.

The cognitive impairment is next most common, occurring in about 70% to 90% of cases. And then urinary dysfunction in a similar number of people. The complete triad is always seen about 1/2 the time or maybe up to 2/3s of the time. And then about 70% to 80% of people may have only two of the symptoms.

So when describing the gait disturbance, usually, people have a small-stepped gait or a magnetic gait, where their feet are stuck to the floor. As well as a broad-based gait, as they're trying to stabilize themself from the imbalance. The strides can become shorter and we're seeing instability, especially during turning. So the patients have a lot of dysfunction during turns, as well as changing position from sitting to standing.

To differentiate from Parkinsonism, there's usually little benefit from external cues, such as verbal commands or visual markings. What's critical is to have an improvement after the CSF removal in a lumbar puncture or lumbar drainage trial. Afterwards, the patients usually have an increased stride length, and a decreased number of steps during turning. And then there can be also be some improvements seen in the leg elevation or instability.

In terms of the cognitive impairment, people primarily have issues with frontal lobe-related functions. Usually, problems with psychomotor speed, attention, and working memory, as well as some problems with verbal fluency. Severe idiopathic NPH shows an overall cognitive impairment. But, usually, these impairments are milder than we see in Alzheimer's disease.

There's also not much of a learning effort as can be seen in other neurocognitive disorders.

Unfortunately, the cognitive issues are sometimes the least predictable to improve. And patients with very severe deficits often showed minimal improvement following shunting. In terms of urinary dysfunction, a lot of patients have symptoms of an overactive bladder. They're usually very bothered by their incontinence, as a lot of them sense that they have the urge to urinate, but have trouble controlling the flow afterwards.

They also note increased nocturnal urinary frequency and urge, urinary incontinence. They also have increased post-void residuals, and reduction of the bladder capacity on urodynamic testing.

There can be psychiatric symptoms, with apathy and anxiety in a large number of patients--delusions, emotional instability, or depression. And then they also can have other neurologic symptoms that can mimic what's seen in other neurocognitive disorders. So there's a fairly large overlap with a lot of the other disorders.

So when we diagnose this, the key finding is diagnostic imaging. So patients need to have an evidence index, which is a measure comparing the width of the frontal horns compared to the maximum width of the inner table of the cranium. And so this ratio has to be at least 0.3 to have the diagnosis.

Going back to DESH imaging criteria. So the classic DESH pattern shows these enlarged Sylvian fissures, as you see on both sides here, as well as on this image. But then at the top of the brain, there's very high and tight convexities as to differentiate it from other diseases like Alzheimer's or just general brain atrophy. So it's a very specific pattern with this enlarged Sylvian fissure.

Again, this image just shows how we can differentiate some of them. So if we look, A, B, and C in these top three rows are all different images showing idiopathic normal pressure hydrocephalus, but with different sized ventricles. And, again, they all have this enlarged Sylvian Fisher fissure, but high and tight convexity.

So this would be the DESH phenotype, as compared to a patient with Alzheimer's, where they do have some ventricular enlargement but it's not to the same degree. But here, we don't see that enlarged Sylvian fissure. And we see more of a frontal atrophy type of picture, with more atrophy along the high convexities.

There's also this entity called LOVA syndrome, which is longstanding overt ventriculomegaly, or also arrested congenital hydrocephalus. So for a long time, before we had high-resolution MRI imaging, this could easily be confused with iNPH. For instance, in this patient, we noticed that they had ventriculomegaly that would be compatible with iNPH. But on this high-resolution MRI, there's actually a cyst at the back of the third ventricle causing obstruction through the aqueduct.

And so these patients present with symptoms very similar to iNPH, but can often be diagnosed a little bit earlier. Sometimes, in the 40s and 50s. But, sometimes, later, in 60s and 70s, as this patient was.

In some of the earlier studies that showed that a third ventriculostomy was very beneficial for iNPH, the thought is that a lot of those patients didn't have high-resolution MRI imaging because it wasn't available back then. And so they are actually likely these arrested congenital hydrocephalus patients.

In terms of other imaging characteristics, so many of the MRI features can actually be corrected following shunting. Although, they still remain with pretty significant ventriculomegaly despite shunting. The posterior half of the cingulate gyrus can be narrower than the anterior half. And then there's newer measurements looking at callosal angles. Or, more recently, the interior colossal angle in terms of predicting response to shunting.

People have looked at other imaging modalities, such as phase contrast MRI, looking at CSF flow. There's been some research here looking at that that has shown some benefit in its diagnostic use. But the data is really inconclusive right now.

People have looked at lactic acid peaks in MR spectroscopy, but that hasn't been found to be consistently diagnostic either. Additionally, looking at increased perfusion at the convexities, or to try and differentiate it from other forms of dementia. But, again, there's fairly limited data on that.

The CSF removal test is really one of the key diagnostic functions. So there's either a lumbar puncture, which is a high-volume lumbar puncture of 30 to 50 ccs, versus a large-volume lumbar drainage trial, in which a lumbar drain is actually put in for a couple of days. And the patients drain at 5 to 10 ccs per hour for a number of days.

The lumbar drainage trial for several days has higher sensitivity and specificity. But it has a

complication rate of almost 10%, which can be from disconnection, radicular pain, or infections leading to meningitis. The CSF needs to be colorless, watery, and clear. And the pressure is less than 25 centimeters of water, less than 20 millimeters of mercury.

There is some evidence that people have looked at measuring different proteins in the CSF, such as neurofilament light chain or beta amyloid, and looking for high levels of leucine-rich glycoprotein. But a lot of this data is somewhat inconclusive still.

In terms of assessments-- so there's a lot of assessments that people have used to follow this, but, unfortunately, nothing standardized at this point. In terms of the gait, a lot of people do 3-meter timed get-up-and-go tests, where the patient stands up from a seated position, walks 3 meters, turns around, and sits back down. So that measures their sit-to-stand transition, as well as any issues with gait, as well as turning. Additionally, there's a 10-meter straight walk test, where the gait velocity is measured.

In terms of the cognitive assessment, a lot of people use a mini mental status exam, but it's a very insensitive test and you need to have a fair amount of dysfunction before things are picked up on that. There's also other frontal assessment batteries, trail-making tests, and then the modified Rankin scale can be used for global outcomes.

There was recently the iNPH scale scoring system that was created several years ago by a multi-center group, in which a lot of these scores of these different tests can be converted to a standardized score for urinary dysfunction, cognitive dysfunction, and gait dysfunction, to, at least, have somewhat more uniform measures or a way to convert these stories. So, again, there's a wide differential diagnosis in these patients. And there's a lot of overlap with other things such as Alzheimer's, vascular dementia, Parkinson's disease, progressive supranuclear palsy, multiple-system atrophy, and other secondary hydrocephalus causes. And so, again, sometimes, it's hard to really tease out if there's one diagnosis. And there can be multiple diagnoses in some of these patients.

So this is a good representation of the treatment algorithm when thinking about these patients. So, again, they need to be at least 60 years old to have iNPH, at least one symptom, primarily-- at least, gait-- and then, additionally, either cognitive or urinary dysfunction, or all three. No other causative neurologic or non-neurologic disorders that would explain it. Again, dilated ventricles with the least an evidence index of 0.3 on CT or MRI, and no other apparent disorders that would lead to hydrocephalus.

So at that point, they can do this with MRI to figure out if they have DESH or non-DESH imaging. There is some data that the DESH patients have a better outcome in terms of their improvement. At that point, I think the first line is to do a lumbar puncture of 30 to 50 ccs. Make sure that agrees with the intracranial pressure scores of less than 20 millimeters of mercury, as well as a normal CSF profile. And then do assessments before and after the lumbar puncture.

If there is concern and you have high suspicion, but they don't have a substantial improvement-- which some of the patients do, who have had significant problems for a while. Sometimes, they don't have as great of an improvement. Then you could go to a lumbar drainage trial for a couple of days and see if they do have an improvement.

If we do see an improvement following these CSF drainage trials, then they become a candidate for shunt surgery. But it really doesn't become a definite diagnosis of iNPH until you can document there's an improvement following the shunt surgery.

So right now, unfortunately, surgical intervention is the only treatment supported by high-quality evidence. So there was the SINPHONI trial that was published several years ago, showing improvement following shunting. But there still remains some skepticism, especially in neurology world, about if this diagnosis is valid as there hasn't been a clear randomized trial looking at shunting versus non-shunting.

So, currently, there's the PENS trial, which has recently been started, in which patients are getting a newer type of shunt that has a virtual offsetting. And all patients are getting the shunt put in, but one group is in the virtual off position for the first several months. And then they'll have it turned on later to really be able to show that there is a difference following shunting.

The surgical procedures can be either a VP shunt, which is down to the abdomen, ventricular atrial shunting, where it ends at the heart, and there's ventricular pleural shunting or lumboperitoneal shunting. Really, there's been a lot of smaller studies comparing one versus the other, but no great studies can comparing the surgical procedures. So, currently, any of these would be an acceptable treatment. But, really, in most people's minds, VP, VA, and LP shunting are really the main standards of first-line treatment, depending on the surgeon's preference.

A programmable valve is usually recommended in these patients due to the significant risk of

over drainage with a subdural hematomas. Again, people also recommend having an antisiphon, in which it prevents sucking a fluid from a negative pressure at the distal end of the tubing to, again, prevent over drainage.

Despite all of this testing, really, we say about 80%, sometimes 90%, of the patients have improvement after shunting. But we haven't been able to come up with a great diagnostic criteria to really get it closer to 100%. And then, as I discussed before, ETV-- or third ventriculostamy-- is not recommended for iNPH treatment. But it would be for more of the obstructive causes of the arrested congenital hydrocephalus.

So there's been some working at trying to come up with initial shunt settings. One group created parameters based on height and body weight to try and come up with the ideal shunt setting to start with. But a lot of people with programmable valves started around a mid setting, just to minimize the risk of overdrainage. And then you can dial that down over time to increase the drainage.

In terms of post-operative care, so initiation and gait retraining in physical therapy is usually important. A lot of these patients have significant gait and balance issues. So it's very helpful to have physical therapists involved to teach them techniques to improve their symptoms afterwards. Again, it's good to start with a moderate to higher pressure setting, and gradually lower this during follow-up to prevent overdrainage.

I perform CT studies after surgery to make sure there's no bleeding or any complications with catheter placement. And then a one, six, and 12 months, or with clinical worsening. Some people have a lower schedule or more frequency tease as well.

If the symptoms persist at the setting you start at, you can then turn it down a couple of millimeters or one setting, and follow up in two to three weeks. And then can repeat as needed to try and improve their symptoms. If there's still no improvement after really dialing their shunt down, then you can consider shunt patency test to make sure that there is actually still flow through the shunt.

In terms of complications, infection is a significant one. But in our series at Johns Hopkins, this is usually around 1% or less. There's shunt failure, which has been as high as 30% to 50% at two years in some studies. And in which case, you can do a revision and often recover their improvement from shunting.

Some patients do get headaches following shunting-- whether that's from overdrainage-- and having low pressure headaches when they stand up. Or just headaches from the incision. And then there's a 3% incidence of subdural hematomas and hygromas, which are the more significant complication of overdrainage.

At this point, you can either consider dialing it up. And if it's already maximized, sometimes, you have to ligate the shunt if it's at the maximal setting, or with some of the newer valve types that can be almost turned off.

In terms of looking at the outcomes, we have found-- in a prior study-- that patients who have long-standing symptoms may take longer to demonstrate improvement. But by around six months, all the patients ended up around in the same improvement.

In terms of gait disturbance improvement, usually, that's about 60% to 90%, often within two months, but certainly about 95% up to one year. Again, the dementia improvement is 30% to 80% with a wide variation, depending on which scale is used. But, again, a lot of these scales are not very detailed psychological assessments. So our tools are, right now, fairly crude. So I think it's hard to pick up some of the more subtle improvements.

And then urinary incontinence, also, has a fairly large range of improvement. But, also, because a lot of these patients are elderly people who may have other issues, such as prostate issues, that could also lead to urinary dysfunction.

But I think there are a lot of future areas for growth and research. A critical one is to really better understand the mechanism of idiopathic NPH. Also, coming up with better modalities for diagnostic imaging, more specific and standardized cognitive testing, as well as standardized gait testing.

When we should perform the diagnostic testing after the lumbar puncture. Hopefully, coming up with better CSF protein markers that would be predictive of who will be a shunt responder. When to do shunt setting changes, and how to minimize infections and other complications.

So now I'll transition over to talking about idiopathic intracranial hypertension. So this is one of the other more common adult-onset hydrocephalus types, although, there are pediatric patients with it as well. It's a relatively rare disorder in the general population. But it's characterized by signs and symptoms of elevated intracranial pressure, a normal CSF profile, and at least pressure of 25 millimeters of water in their lateral decubitis position without any

identifiable cause found on neuroimaging. So, again, it's an idiopathic form.

So this was first described as meningitis serose back by Quincke many years ago. And then the other term, pseudotumor cerebri, that's fairly commonly used in the literature was first coined in 1904. And this was increased intracranial pressure without an identifiable mass lesion. Idiopathic intracranial hypertension is the more accepted term right now. And this was first coined back in 1937.

So, again, benign intracranial hypertension has also been used frequently. But, usually, this is discouraged as this condition is not really benign and people can have fairly severe visual problems from this. Again, PTC or pseudotumor cerebri and IIH are often used interchangeably. But, currently, the IIH-- or idiopathic intracranial hypertension-- is really the preferred nomenclature.

So, currently, it's an important area of research and investigation, especially with the rising prevalence of obesity. So, currently, the economic costs of this disorder exceed almost $500 million a year. There's frequent hospital admissions for these patients, fairly unsatisfactory treatment options, and lost productivity of young patients that should be contributing to the workforce at that age.

There have been some recent guidelines that were just published in JNNP recently for the diagnosis and management of this disorder. So looking at the epidemiology, the annual incidence is pretty rare in the general population, about one in 100,000. This goes up to 3.5 in 100,000 in women. So it is much more common in women as compared to men. And this is young women-- 15 to 44.

However, when we look at people who are more than 20% above ideal body weight, this goes up to almost 20 in 100,000 in that young female population. And the higher your BMI gets, the greater the risk of IIH. Even non-obese patients with a BMI of less than 30 are at greater risk if they had a recent moderate weight gain of 5% to 15% of their weight.

When we look at the pediatric population, boys and girls are affected equally before puberty, while we get this female predominance later. And this goes up to almost a nine times higher rate in women compared to men. And this very rarely develops in patients over age 45.

Unfortunately, the pathophysiology of this is still unclear. Some thought that there's increased brain water content with increased brain compliance that prevents hydrocephalus or

expansion of the ventricles. There's some thought of excess CSF production, reduced absorption of it. Increased cerebral venous pressures has been more commonly looked at now, as well as some other relationship with aquaporin-4, which is involved in brain water homeostasis.

And there's also some association with the transverse sinus and sinus stenosis. So we do know that when there's increased intracranial venous pressure, which can be often from stenosis of the distal portion of the transfer of sinus, this can prevent CSF drainage, which goes into the distal sinus via arachnoid granulations. It's also possible there is microthrombosis that we don't pick up on our imaging, and cerebral veins, which can result in impaired CSF absorption.

But some of this-- as you can see, there's a cycle in which there's sinus stenosis with problems with outflow obstruction leading to venous hypertension, decreased CSF absorption, increased intracranial pressure. And then we know with increased intracranial pressure, there's increased compression of the sinus. So you get this vicious cycle and it's unclear what comes first.

Like the chicken or the egg. Do you have impaired stenosis in the sinus that leads to this? Or is it that there's increased pressure from another thing compressing the sinus and causing the cycle to get worse?

So transverse sinus stenosis has gained increasing attention, probably, over the last 10 years. And, again, it's very unclear if this is incidental or secondary to the increase in intracranial pressure, or the causative mechanism. And it may be some component of all of these.

It can be related to the presence of some trabeculations or septum or larger arachnoid granulation compression. And, again, we've also seen other studies where it's related to increased intracranial pressure actually compressing the sinus. And there has been a study showing complete reversal of the sinus stenosis after a lumbar puncture, when the pressure was decreased. And it can also be found, incidentally, in patients who don't have high pressure in their head.

But, currently, in looking at diagnostic criteria for IIH, there are several criteria. So, one, that the symptoms only reflect those of elevated intracranial pressure or papilledema. The signs are only attributable to increased intracranial pressure or papilledema, documented elevated intracranial pressure during the lumbar puncture, normal CSF composition. And then no

enlarged ventricles, intracranial mass or structural vascular lesion that would explain this, and no other cause, such as sinus thrombosis, that would explain it.

So in terms of diagnosis, these patients usually come through either ophthalmology or neurology. Usually, a clear history and physical needs to be performed to see what the onset of the issues are. But most of the patients either present with headaches or visual dysfunction.

An MRI, as well as an MR-venogram, should be performed to rule out sinus stenosis or sinus thrombosis. And this is followed by a lumbar puncture and CSF analysis, as well as a formal ophthalmology evaluation to check for papilledema and see what the baseline visual fields and that visual acuity are like.

So this kind of shows a good diagnostic flow. So once papilledema is identified-- usually, by the neurologist or ophthalmologist-- again, they need to have a formal ophthalmology evaluation to document a baseline exam, as well as checking blood pressure to make sure there isn't extremely elevated blood pressure and malignant hypertension. And then they should have brain imaging with CT or MRI to rule out any other pathology, as well as venography.

And then, once no lesions have been identified that would explain it, a lumbar puncture will be next. Again, if the pressure is elevated above 25 centimeters of water and they have a normal CSF protein, glucose, and cell count, at that point, you exclude secondary causes. And it can be diagnosed with idiopathic intracranial hypertension.

This can then be further classified in a fulminant, typical, and atypical. So in fulminant IIH, these are the patients that come in with acute, severe vision loss that's rapidly progressive. And these are at emergency, in terms of treatment, to save their vision.

And then in typical in IIH, this is usually a woman of reproductive age with a BMI above 30. In atypical, it's either the person is not female-- so all the males are classified as atypical-- older, or not of reproductive years. Or patients who are non-obese with a BMI of less than 30.

In terms of the clinical manifestations, there's a lot of symptoms that they present with. It's primarily headache and visual dysfunction. But some patients complain of intracranial noises, visual loss, diplopia, as well as some paresthesias or radicular symptoms. And psychiatric pathology and then papilledema that goes with the visual dysfunction.

In terms of the headache, almost all patients have headaches. And this is, usually, the presenting symptom. It's typically daily. It can be retroocular and worsens with eye movement. Some report increased severity when awakening as they've been lying flat all night. Some people describe throbbing in association with nausea, vomiting, or photophobia.

So it can often resemble a migraine. And it becomes more challenging because a lot of these patients do have coexisting migraine disorders. So it's very hard to sort things out in a lot of these patients. The chronic daily headaches can also be related to analgesic overuse, which a lot of patients have from these chronic headaches.

In terms of the transient visual symptoms, these are commonly experienced in up to 75% of patients. Some believe it's a manifestation of disc edema that leads to transient ischemia of the optic nerve head. Patients can have brief episodes of one or two eyes with visual loss that can be partial or complete. But these, typically, last only seconds, and don't necessarily correlate with the degree of disc edema or visual loss.

Pulsatile tinnitus is one of the most common intracranial noises with ringing in the ears. This happens in about 60% of patients. But about 10% of normal controls can also have this finding. It can be unilateral or bilateral, and is often described as a heartbeat or whooshing sound.

Interestingly, it often goes away following a lumbar puncture or jugular venous compression. Some people think it's from transmission of intensified vascular pulsations via the spinal fluid under high pressure to the walls of the venous sinus. And that leads to some turbulent flow, causing the noise.

In terms of visual loss, this is really the critical and threatening symptom in this disorder. So, usually, some subjective visual loss or blurred vision is the presenting initial symptom for a lot of patients. There can be a dark spot, temporally, that correlates with enlargement of physiologic blind spot, as well as tunnel vision. In severe cases, there can be profound visual loss or even blindness. In patients with fulminant IIH, this can progress very rapidly-- over hours or even days.

Diplopia, or double vision, is commonly reported, as well, in about 30% to 60% of patients at presentation. It's, usually, in both eyes in a horizontal diplopia. It's often from a unilateral or bilateral sixth nerve palsy. This almost always resolves when ICP is normalized. It can also come from macular edema or exudates with severe papilledema.

A lot of these patients do have psychiatric pathology, with depression and anxiety being more common in patients with IIH than in controls. It's unclear if this is related to the pathogenesis of IIH, or that having these chronic headaches and symptoms lead to more problems with depression and anxiety. And so all these patients see multiple providers before this diagnosis is obtained.

Now, so papilledema is really one of the hallmarks of IIH. And it can often be asymmetric. There is an association between visual loss and high-grade papilledema, or even optic atrophy. But the appearance of the optic nerve does not necessarily predict visual outcome in the less severe cases.

So, again, the visual assessment is the critical thing at baseline and in follow up and treating these patients. So about 15% of patients do have visual acuity worse than 20/20 at their initial visit. Contrast sensitivity is usually pretty sensitive, an early indicator of optic nerve dysfunction.

The color vision is not necessarily sensitive. The presence of an afferent pupillary defect can be found in asymmetric visual loss, but it's often absent in these patients. Perimetry is a very useful test for evaluating visual function and checking the visual fields. The visual field defects are very similar to what's seen in other causes of papilledema.

Usually, the most frequent field abnormalities are a blind spot enlargement, generalized field constriction, and nasal defects. Optical coherence tomography, or OCT, is a newer modality measuring the thickness of the nerve that's been very helpful, and is getting more widely used now.

So, again, these are some representations of the field testing here, which shows the enlarged physiologic blind spot, as well as the inferonasal depression. And then, here, it shows just a generalized constriction with the only remaining good vision in the center of the visual field.

So neuroimaging, again, is mandatory before moving on in the workup, as you need to make sure there's not ventriculomegaly or another source-- such as a tumor-- that's causing the problems. The patients often have very small, slit-like ventricles. And, again, MRI is usually the preferred imaging modality, including an MR-venogram. But if MRI is unavailable, or the patient has implants that preclude its use, then a CT with contrast is recommended.

So these are some of the common MRI findings that are found, including this hyperopic shift in the optic nerve, as well some flattening of the globe posteriorly. Other patients will have an empty sella, seen here. Or, again, transverse sinus stenosis is very common. But this is some of the things that need to be ruled out. So this shows gagittal sinus venous thrombosis, in which the main draining vein at the top of the brain is thrombosed, waiting to elevate at pressure due to impaired venous drainage.

So the CSF exam, again, is critical for this as well. And the accepted diagnostic pressure, currently, is more than 25 centimeters of water or greater in adolescence and adults. In kids it's actually greater than 28 centimeters of water. And values in that 20 to 25 range can be non-diagnostic.

But the pressure has to be measured in the lateral decubitus position, with the legs relaxed, for it to be a true pressure. As the ICP can rise if they're not in this position-- if they're prone, or under anesthesia, or in pain during a procedure. And, again, the fluid is usually analyzed for glucose, cell count, different cultures, and cytology.

In terms of pregnancy, the rate of onset of this is similar to non-pregnant controls, but the disease can develop or worsen during pregnancy. Yet, the diagnostic criteria are the same in pregnancy. Diamox, which is one of the mainstay medical treatments of this, is safe to use after 20 weeks of gestation. But the thiazide, diuretics, or tricyclic antidepressants, which are farther down the line, should be avoided in pregnancy.

There is no contraindication to optic nerve sheath fenestration or shunting during pregnancy. Though, there is a theoretical risk of catheter malfunction with a peritoneal catheter from the enlarging uterus. And, I think, a lot of surgeons are nervous implanting a peritoneal catheter in a pregnant patient.

However, if this disorder arises in the immediate postpartum period, this should really raise your suspicion for venous thrombosis instead, as patients can be hypercoagulable. I'm looking at children and adolescents. So, again, it's an equal prevalence among boys and girls in pre-puberty. But among adolescents, girls are more commonly affected.

Obesity is not necessarily as prevalent in the pediatric population, but we are seeing it more as the pediatric population does have increasing issues with obesity. Secondary cause is found in a lot of these patients-- in up to 50% of cases-- with other predisposing conditions such as ear infections, viral infections, medications, as well as head trauma.

Papilledema can be absent in the young population. The fontanelle is still open. Often, people present with stiff necks, strabismus, irritability, apathy, dizziness, and ataxia. And if this is an idiopathic onset, again, the treatment is the same as in the adult population.

So when looking at the treatment, really, you need a multidisciplinary team, involving neurologists, ophthalmologists, neurosurgeons, and primary care physicians to manage these patients. When we think about that treatment paradigms-- so, again, weight management is a critical thing. With weight loss, a lot of the headache and visual symptoms do improve. So some advocate that even looking towards bariatric surgery is a strong consideration for these patients.

So I'm looking at these. So, again, the visual dysfunction is the key criteria. If there's no immediate threat to the vision, then one can consider medical therapy with Diamox or acetazolamide. If the vision is threatened and it's an acute loss in this fulminant IIH, then either a temporizing lumbar drain should be inserted, or definitive treatment with CSF diversion, with a shunt or optic nerve sheath fenestration. We've had limited success in the past in putting a lumbar drain in some of these patients, then looking towards venous sinus stenting. Then published a small series of patients that had good outcomes following this approach.

In terms of medical management, again, weight loss is a significant thing for obese patients to consider. In a prior study, where they looked at some morbidly obese patients who had weight loss of an average almost 60 kilograms by bypass surgery, they had resolution of the papilledema and headaches following this. Even in another analysis of 58 women, there was improvement of papilledema grade, as well as visual fields in those who at least had a 2 and 1/2 kilogram weight loss over three months.

When looking at pharmacologic therapy, again, Diamox is one of the main treatments. This leads to decreased secretion of CSF from the choroid plexus. It can be effective in about 75% of patients with IIH, at a dose of 1 to 4 grams a day in divided doses.

Almost all the patients, especially at higher doses, can get paresthesias, altered food taste, and low serum bicarbonate levels. Also, some patients with sulfa allergies don't tolerate it.

Lasix is another one that's been looked at as a second-line treatment. And then corticosteroids can lead to rapid decreases in ICP, but you can't really use them chronically. In terms of the headache treatment-- so this is a treatment similar to what's used in migraines, with tricyclic

antidepressants or valproic acid. But these can often lead to weight gain, which can worsen the problem.

Calcium channel blockers, beta blockers, or Topamax. And this one can actually be helpful, somewhat, with weight loss as well. Triptans and dihydroergotamine can be used if they do have a concomitant migraine disorder.

In terms of surgical treatment, optic nerve fenestration is one of the mainstays. And this, primarily, helps patients with visual loss, but it doesn't really help with the headaches. The mechanism of this is still fairly poorly understood, but there's some thought that it increases blood flow to the optic nerve and may lead to a global decrease in ICP.

It's generally effective, but usually requires a revision. It's more effective when there's acute papilledema rather than chronic papilledema. And it does have about a 35% chance of failure from three to five years post-op.

CSF shunting is another mainstay of treatment. The ventricles are not large. They're very small in these patients. So some prefer lumboperitoneal shunting. Otherwise, usually a frontal shunt is used if it's inserted cranially due to the small size of the ventricles.

It's usually a curative procedure for both the headaches and the visual dysfunction, but it has significant complications. In looking at a series of 27 patients, there was a 100% success rate in the first two months of treatment. But over 50% needed between one and 13 revisions over 21 months of follow up.

In another series of 37 patients, 27 of the shunts were placed within the first two months. So there are fairly significant issues with shunting. Even in LP shunting, there is about a 50% failure rate. And the lumboperitoneal shunts can also lead to a worsening of Chiari malformations in these patients.

In acute vision loss, there is a small subgroup-- again, with fulminant symptoms-- which lead to this precipitous visual decline. And this really requires rapid and emergent treatment, whether it's optic nerve fenestration or temporary lumbar drainage, until a more definitive treatment is offered or a shunt placement.

Transverse sinus stenosis is, again, gained increasing examination over the past several years. One study found that over almost 90% of the patients may have it. Other studies have shown more it's in the 30% to 70% range. Again, it's unclear if the elevated ICP leads to this,

or if sinus stenosis is the primary pathogen.

In looking at one of the series, they found that 78% of patients had improvement of chief presenting symptoms, whether headache or visual dysfunction. And 85% with improvement in papilledema following stenting. There was a large series out of Australia with 52 patients. And they found that they only required unilateral stenting. And when checking the intracranial pressure, the CSF pressure decreased from a mean of 32 to 22 following stenting.

But it's critical that there is a pressure gradient across this to stenosis, usually of at least 8 to 9 millimeters of mercury, for someone to be a candidate for this, in addition to having the stenosis. There, also, can be a rate of re-stenosis adjacent to the stent. So they did find that about 10% of the patients had this. Since then, they've started using longer stents that decrease that rate of adjacent segment stenosis.

There are reported issues and complications with this. One is that this treatment requires dual aspirin and plavix antiplatelet therapy, usually with a couple day load. Again, there's about a 10% to 12% revision rate. A lot of patients do get frontal headaches, which is thought to be due to dural stretching by the stent, that do resolve over about a week.

Patients have reported transient hearing loss. There's also been complications of the guide wire perforation during the endovascular procedure, which leads to a significant intracranial hemorrhage. And, additionally, this can be compounded by being on the heavy antiplatelet therapy.

So what's the best treatment? Currently, that's still unclear, unfortunately. There's a site study that's been recently started, which we're participating in here. This is comparing optic nerve sheath fenestration versus VP shunting. Unfortunately, there is no arm for venous sinus stenting. But many centers are participating in this study as well. So, hopefully, this will at least provide some more insight.

My own personal opinion is if they failed medical management, I think weight loss is a very critical one. I think that's really one of the only truly curative aspects for the patients with typical IIH and considering bariatric surgery.

Venous sinus stenting, I think, is an excellent option if sinus stenosis is present, as shunting, I think, is more of a last resort. Or if emergent treatment is required, as the complication rate and failure rate is just very high in these patients. Again, optic nerve sheath fenestration is an

excellent option, especially if they have visual symptoms with a less prominent headache.

But, really, I think this requires a multidisciplinary team for optimal treatment. Usually, avoiding and treating the visual loss is the primary management goal. And I think some surgery is really more of a second-line treatment for patients with persistent or recurrent venous sinus stenosis, or fulminant IIH that requires more emergent treatment. But even after treatment, due to high failure rate of, really, of all these treatments, they still require a very close follow up, especially in their visual function.

So, lastly, I wanted to touch base on some of the surgical procedures and technical considerations in terms of shunt placement and the treatment of adult hydrocephalus. So, again, CSF shunting-- especially ventricular peritoneal or VP shunting-- is the most common procedure for these patients. And it's useful for, really, all types of hydrocephalus.

But there are a lot of complications, including failure, obstruction, infection, and other shunt-induced complications. So especially in the NPH patient, there's long-term complications, with underdrainage of CSF-- in which the symptoms don't improve-- overdrainage of CSF-- in which they can get-- or the static headaches or, in the worst case scenario, large subdural hematoas, mechanical failure, malposition or break of the tubing, CSF leaks, or even seizures and infections

Unfortunately, several studies have shown that about 70% to 80% of all patients with shunts have at least one revision at some point in time. This is probably heavily skewed towards the peds population, where some of them can have well over 100 revisions over time. And, unfortunately, despite some advances in shunt technology, it's still a relatively primitive technology that dates back 40 or 50 years.

In terms of the general surgical principles in these patients, I think a lot of patients need a fairly wide shave around the area of incision to minimize the risk of infection. My practice is to scrub the incision and any areas that will be exposed during the procedure for five minutes, with either providone-iodide or chlorhexidine. And then a double layer of draping with the providone-iodine impregnated sheets. And then giving preoperative antibiotics, and then peri-op antibiotics for 24 hours following shunt placement.

In terms of post-operative care, most patients go to the recovery room and they're admitted for overnight observation. I like to get shunt series X-rays at baseline, as well as a baseline head CT. Or a chest X-ray if an atrial or pleural distal catheter is used.

In terms of ventricular catheter placement, there's three options. One is the standard frontal placement at Kocher's point. There's also the parieto-occiptal approach, which places the catheter in a similar position to try and avoid the choroid plexus. And there's also a parietal approach to the atrium, which is often the most dilated portion.

In terms of ventricular catheter placement-- so the frontal incision, again, for frontal placement are usually a retroauricular incision. At that point, a subgaleal pocket, as shown in this image, is created to house the valve and reservoir, because you don't want it immediately underlying the incision, where it can lead to break down of the incision and increase risk of infection.

The catheter is usually trimmed at about 5 to 7 centimeters for a frontal approach, and about 9 to 11 for the posterior approach. And, usually, you want to confirm that there is good flow from the distal catheter before you place it into the distal insertion site.

So we have found that the location of the catheter is correlated with rate of malfunction. So it's about a 20% failure rate if the catheter is placed well and entirely within CSF. But this goes up to 33% if it's only partially in CSF. A freehand placement of the frontal catheter is usually fairly straightforward, except if the patient has very small ventricles, such as in IIH.

But the parietal-occipital approach has a much smaller margin of error. And if you're very experienced, some people have great success doing it by a freehand approach. But with our navigation technology now, that's usually a preferred method for placement so you can get a fairly optimal placement.

So image guidance has been increasingly used, especially in patients with small ventricles or slit ventricle syndrome. MRI can be used but, usually, a CT is more than adequate for these patients and less expensive. In most of these, the patient is positioned and registered to a navigation system. There's older frame-based approaches, and the newer frameless ones. Both that require a Mayfield clamp, as well as newer ones with just a marker that's placed on the forehead.

In terms of image guidance outcomes-- so we looked at this previously in the NPH group and found that with a very experienced surgeon, that didn't provide much benefit. But in using it in the pseudotumor experience with very small ventricles, MRI guidance was used in frontal ventricular catheters. And all of these were successfully placed in slit ventricles with a single pass.

Another group had similar experiences in children with slit ventricle syndrome, with no revisions of the proximal catheter in the eight-month follow-up period. Another group looked at a series of 21 adult and pediatric patients and found that they still had very rapid operative time of about 46 minutes. And 20 out of 21 had excellent catheter position entirely in their CSF, and one had it partially in the CSF.

There are downsides to this. Again, one is the cost. It's an additional scan and use of the equipment. Potentially, somewhat of an increase in operative time, as well as increased billing if neuronavigation is used. Theoretically, there would be a potential increase in infection from the couple extra minutes of operative time, but I think that's pretty minimal.

And then, depending on what navigation system you use, there's potentially exposing drapes to the non-sterile hardware towards the end of the drapes. But I think these are relatively minor problems. There can also be problems where the registration and accuracy is not foolproof, so you still have to use your own surgical judgment for these.

There are alternatives. So you can do this endoscope assisted, in which you use a rigid or flexible endoscope as the stylet to visualize that you are in the CSF space. Some people have had success with ultrasound guidance in infants with open fontanelles. And others have shown that this can be adapted in older children using a larger burr hole.

People have looked at using a peel-away sheath, which is used in a lot of other procedures. And passing the catheter through this can avoid placing it through the brain parenchyma, which might help with preventing proximal malfunctions, as the catheter can get clogged with some of that brain parenchya. But this has not really been widely adopted at this point.

In terms of shunt technologies, they're all pretty similar, where there's a proximal or ventricular catheter then connected to a reservoir and a valve that regulates flow, followed by a distal tubing that goes into either the atrium pleura or peritoneum. There's been multiple different proximal catheter technologies tried over the years. But, really, the mainstay is a straight ventricular catheter.

A lot of these other designs have been used in the past, such as this flanged or the Fuji basket. Or recessed holes to try and prevent choroid plexus clogging up these holes. But a lot of these have actually made it much worse and are very dangerous to remove.

So, again, proximal catheter occlusion is a big problem, more in peds as compared to the NPH population. And this, usually, results from obstruction in the proximal catheter tip from choroid plexus or ependymal tissue. The catheter can be very difficult and, sometimes, dangerous to remove. And you can get significant bleeding within the ventricle if it's still very adherent to some those structures.

So one of the tricks is to stick a metal guide wire or stylet, that can then be coagulated, to try and get some of the debris or choroid plexus to release and prevent bleeding. When looking at the shunt valves-- so there's, usually, two different mechanisms. One is either a ball and spring, which a lot of the shunts use, versus a silicone membrane. There's an assortment of programmable valves, as well as other methods to prevent overdrainage or underdrainage.

So this list, I guess, doesn't project very well. But there is well over 100 different types of valves that have been used over the years. So this just shows some of the different ones that we commonly use that all have pretty similar technology, with a reservoir that's connected to the ventricular catheter and then some sort of mechanism that regulates the flow. And then this one, actually, has an antisiphon device included with the valve. Some of them have it as a separate construct.

So in looking at different valve types, there's usually two different types. One is differential pressure valves, in which they allow drainage once there's a pressure gradient across the valve. But they can result in overdrainage when there's transiently increased ICP from coughing, or negative pressure in the abdomen or pleural space leading to overdrainage and siphoning. There's also flow-regulated valves, which allow for a constant flow rate without a dependence on intracranial pressure. A lot of them do have a safety mechanism that can get activated at very high ICPs, as that function then approaches out of the differential pressure system.

So in looking at the other valve types, there's adjustable valves, which are usually a variation of differential pressure valves. And they allow percutaneous adjustment of the pressure, usually with a special magnet. Some of them have to be reprogrammed for MRI, and some of them can actually be affected by household magnets or electronics.

There is a study on this strata valve that show that the iPad, in close proximity, could actually change the setting. Then we recently had a patient here, who worked with cattle with very strong magnets and has been coming in with changes in their valve setting. Antisiphon valves

are also an important component, especially in the NPH population. This can either be an add-on or built in to prevent the effects of siphoning, where a lower pressure distally can start sucking out pressure due to that differential pressure being achieved from a low distal pressure.

So a lot of this further data came from the group out of Cambridge. So these are some representations of the silicone membrane valve, which is less commonly used over here. This ball-on-spring valve is really one of the more commonly used ones, where a lot of them have a magnetically-movable rotor that changes the load on the spring-- in support of the ball and the cone-- to adjust the flow of CSF.

This shows some of the different pressure flow curves and how they can change with increased resistance. So if there is the distal tubing hooked up, you can see it has a much different flow curve as compared to a distal drain, when there's increased resistance distally. Additionally, there's different flow if the end if it is wet from that surface tension changes, as compared to a dry end.

So the Codman Hakim has been one of the more longstanding programmable valves that has been used. This has a ball-on-spring design and 18 different programming steps. Some of the downsides are it's very sensitive to MRI and magnets. It can be very challenging to reprogram. It can also be damaged by small particles or high protein that can clog it up.

The Medtronic strata is another very commonly used one, which has a ball-in-spring design, usually with a delta antisiphon chamber. And this is adjustable, but is also affected by magnets. And, again, the strata-- these are some of the different flow curves, as they have settings from 0.5 to 2.5. And you can see how the flow and pressure can change at those different settings.

The Aesculap proGAV is another one with a programmable ball-on-spring design. This can be either used with or without this shunt-assist device, which is their version of an antisiphon device. And the programming occurs by turning a rotor within this circle that controls the spring preload, as with most of these ball-and-spring designs. Its can be adjusted from 0 to 20. And this one was one of the original ones that was resistant to changes following MRI or at high magnetic fields.

The Orbis-Sigma valve is another flow control, as opposed to differential pressure valve like the others, which is usually designed to prevent overdrainage. But it does perform pretty

poorly if there's high amplitude intermittent ICP waves.

So in terms of siphoning physiology-- so this is really to prevent siphoning or sucking of CSF from a low distal pressure, rather than a higher proximal pressure. Typically, blood and spinal fluid are at the same hydrostatic level of normal physiology. But in shunting, the CSF is diverted from the craniospinal compartment to whichever distal compartment you're going to.

When the patient's horizontal, the distal spaces are the same hydrostatic levels as the CSF space. But when mobilized, there can be a significant pressure gradient when the patient's upright, leading to siphoning of the CSF to the lower hydrostatic pressure. These are especially pronounced when the pleural catheters are used, as there can be very negative intrapleural pressures there achieved that can really suck out CSF with each respiratory cycle. So it's really critical to use an antisiphon device in these patients.

Again, this shows what happens with the pressures with siphoning. So when the patient is supine, as compared to upright, you can see that significant change with negative intracranial pressure is achieved. So, again, these antisiphon devices are used to prevent overdrainage and are very commonly used in iNPH. And, I think, should be relatively standard care in these patients. They're also commonly used in pediatric split ventricle syndrome patients to prevent collapse of the ventricle.

But in a lot of these, the placement and orientation is critical. Some of the newer designs, not quite as much. Usually, these have a mechanism, where they block drainage once that distal suction pressure exceeds the intracranial pressure. Usually, you need them in a vertical orientation close to the level of the foramen and Monroe, which is around the extra auditory meatus. But some groups have found lowering placement by about 10 centimeters is still acceptable.

So this is the Codman siphon guard, which is found on the distal end of a Certas, or it can be a standalone. And you can see how it changes, when this activates on this flow pressure curve. But, sometimes, people have found this switching between these channels can be unreliable.

Aesculap, with their program system, actually came out with the ProSa, which is programmable antisiphon device, several years ago. And some people have been using that more commonly. The horizontal vertical valve is another type of valve, which kind of has both a horizontal and vertical component built in. And this allows for differential control depending on if a patient's in the upright or supine position, of which one of these kicks in. But the correct

orientation at implantation is critical so it functions correctly.

These are often used with lumbar shunts, but are a nonprogrammable design. Again, this shows what happens, especially in some of the IIH patients with larger body habitus, in which you can place it in the expected orientation. And then it can change significantly despite being sutured in place.

Shunt infections are also a critical issue in shunts. The rate is 5% to 10% in adult literature. At Mayo and the Johns Hopkins experience, it was, usually, around 1% or less. It's, typically, found within the first several months after implantation. And can arise from bacterial colonization of the hardware, usually from contact with the skin of skin edges. Due to the foreign body, usually the normal immune response that would be used to clear it is blunted, and patients can develop a biofilm. So, really, hardware removal is critical if this occurs.

Patients often present with signs of meningitis or things like headache, nausea, vomiting, or abdominal pain. They, also, can have erythema or inflammation along the catheter tract, wound dehiscence or discharge, or abdominal fluid collections or pseudocysts.

Another group published a shunt insertion protocol that decreased their shunt infection rate from 8% down to a 0.2%. A lot of these things are trying to complete the procedure faster-- opening up the presterilized shunt components right before use and soaking them in antibiotic impregnated irrigation, exposing the minimal area needed to complete the procedure, as well as the abdominal dissection occurring before the cranial incision to minimize the time of the cranial incision.

Some other modifications that other people have used are keeping the same scrub team present throughout the procedure. And, essentially, locking the doors to minimize flow in and out of the room. Making sure all staff are on the same page of the standardized protocol, continuing antibiotics an additional 48 hours-- but that has more controversial data-- and then, again, the wide shave and five-minute scrub.

In terms of perioperative antibiotics, generally, most people will give a dose within one hour of incision, and then 24 hours postoperatively. Usually, there's very little data to support continuing them past 24 hours. The antibiotic-impregnated shunts have become increasingly popular throughout the past several years. The Codman and Bactiseal and the Medtronic areas are some of the more commonly used ones, in which both the proximal distal catheters

are impregnated with antibiotics-- with rifampicin and clindamycin. And they have prevented bacterial adherence and colonization in the shunt hardware.

In the peds population, we found that there was a decrease in infection rate from 12% to 1% over a six-month follow-up period. In the adult population, where the baseline was lower, was about a 4% to 1% decrease. Another study found there was no difference in infection rate when using these. But in their study, the baseline infection rate was substantially higher than in most other series that may have wanted the response.

There has been concern that you're selecting for resistant bacteria. But, in another study, they found that there were similar rates of MRSA infections when using both the antibiotic impregnated and non-impregnated. So if they do get a shunt infection, IV antibiotics alone are not sufficient to get rid of the infection. These require hardware revision and replacement.

If the patient is shunt-dependent, as in some of the congenital hydrocephalus, you need to externalize the shunt. Or remove everything important and put in a ventriculostomy catheter for usually about two weeks of IV antibiotics before replacing everything. In patients with iNPH or IIH that's not fulminant, you can remove the whole system completely and treat them with antibiotics before replacing it.

Unfortunately, shunt infections due cause a lot of morbidity. In pediatric patients, there is a 12-day mean hospital stay-- an average of three shunt surgeries, four CT scans, and six X-rays, at a mean hospital cost of $50,000 per patient. In adult patients, the hospital costs is about $40,000. The antibiotic-impregnated catheters do have a higher initial cost of about $400 versus $150. But the cost savings is estimated to be about $25,000 to $50,000 per 100 patients.

In terms of valve setting, again, underdrainage can lead to persistence of the symptoms, but overdrainage can be a more significant complication in patients. Usually, the optimal setting is the highest setting that still allows for the patient's improvement. In NPH, this is usually an initial setting around the mid-range. In IIH, this is usually more in the upper range.

In terms of valve and setting choice, it's usually a personal preference. And there is a lot of kind of subtle variations between different providers. In adult hydrocephalus, usually an adjustable valve is preferred, but some do still use nonprogrammable valves with good success. The setting can then be optimized over time, and just with a magnet outside the skin.

There's a significantly higher cost of adjustable hardware, somewhere between $3,000 and $4,000 for an adjustable valve vs. $1,500 for the nonadjustable. But a recent meta-analysis that we performed found and almost 30% revision rate with fixed-pressure valves, compared to 10% for adjustable valves in the iNPH population.

Then we looked at our own data at Mayo. There was about a 10% revision rate for nonprogrammable versus 2 and 1/2% for programmable. Again, this shows some significant complications with overdrainage, with complete collapse of the ventricles, as well as a subdural that was then resolved with a programmable valve by elevating the setting without requiring an additional surgery.

Most of these valves are sensitive to external magnetic fields. Though, the newer ones are resistant to that change. So, again, this just shows how the strata will change-- its probability of switch at a magnetic field of 40 milliteslas, much less than the usual 1.5 or 3 tesla MRI fields. It's similar for the Hakim.

And, again, this shows some of the everyday devices, ranging from an electric shaver at 1 millitesla, to some of the induction heating systems, or even cell phones at 17 milliteslas, which is still below the level at most of those should switch. But, again, iPads appear to exceed that, at least for the strata valve. Different ones have different distortion on MRI, which can cloud any further imaging.

But, in conclusion, looking at these, there has been significant progress and success in optimizing shunt placement and decreasing the rates of shunt failure. But, unfortunately, this is still pretty old technology, despite some of the more recent, what I think are more incremental, advances. And we still have a very non-negligible rate of shunt failure and infection that I think we can improve upon significantly.

And some of the future directions, in looking at some of these adult-onset hydrocephalus, I think we really need an improved understanding of the pathogenesis of both iNPH and IIH. Ideally, we need to encourage and develop new and more advanced shunt technology, and even figuring out ways to avoid shunting altogether once we understand the pathogenesis of these better. And, hopefully, continue to strive, to revise, and optimize the surgical procedures and management of hydrocephalus to improve outcome for these patients. Oh, thank you.

[APPLAUSE]